

## What is the definite merit of clonidine premedication in patients with sleep apnea? [Letter]

Axel R. Heller, Carla B.E.S. Henning

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receiving clonidine, being additionally treated with an antihypertensive drug. Because the bispectral index (BIS) was reported to correlate with MAP (3), one could hypothesize that the *a priori* reduced MAP in the clonidine group induced lower (preinduction) BIS values, independent from the sedating properties of clonidine, which, then produced a lower propofol requirement during BIS-guided induction. It may turn out that the clinically small difference of the propofol induction dose  $218 \pm 32$  vs  $190 \pm 32$  mg reflects MAP rather than sedation by clonidine, and the significance disappears when correcting for the systematic confounder, MAP.

To assure between-group comparability, the authors must at least provide data on preinduction BIS values (both groups) and show the independency of BIS and MAP in awake and anesthetized patients at comparable MAC levels. Further, catecholamines increase BIS during general anesthesia (4) and clonidine itself affects catecholamine activity. Although we agree that the use of BIS to titrate propofol is a logical way of standardizing dosage in the operating room, it is not free of systematic artifacts. Including MAP into a statistic model may help exclude potential sources of error. This applies in particular when comparing a sedative with antihypertensive side effects with placebo.

Moreover, surgical effects on the apnea/hypopnea index (AHI) were not considered. In contrast to uvulopalatopharyngoplasty (UPPP) and tonsillectomy (5,6), septoplasty does not reduce the AHI (7). In this regard, the Methods section states that 30 patients were randomly assigned to two groups. Lines 11–14 in Table 1, however, give puzzling numbers. Insinuating the type of surgery as an explicit nominal variable, how can the total number of patients in Group 1 be  $n = 15$  when “septoplasty alone” counts  $n = 12$  and “septoplasty and UPPP” counts  $n = 8$ , and so on? Further, including

the type of surgery into a multivariate model may give additional information on its impact on AHI in the current setting.

Third, it is unclear which data the power analysis is based upon. Nosedá et al. (8) found the reduction of AHI in sleep apnea patients after benzodiazepine treatment. As this trial was designed to establish equivalence or at least noninferiority (safety) of clonidine premedication with regard to AHI, the appropriate statistical test would have confidence interval inclusion. The additional six dropouts further complicate the interpretation.

We also wondered why baseline values of Figure 3c are not given, as these are crucial to assure between-group comparability. We also suggest that the units for the pirritamide dosage in the Results section (Table 3) should read “mg/d” rather than “mg · kg<sup>-1</sup> · d<sup>-1</sup>.”

In conclusion, the data analysis reported by Pawlik et al. does not allow drawing definite conclusions on the merits of clonidine premedication in obstructive sleep apnea syndrome patients, because of uncontrolled confounding factors in a small sample size with a problematic statistical treatment.

Carla B. E. S. Hennig, MD

Axel R. Heller MD, PhD, DEAA

Department of Anesthesiology and Intensive  
Care Medicine

University Hospital Carl Gustav Carus

Technical University

Dresden, Germany

carla.hennig@uniklinikum-dresden.de

## What Is the Definite Merit of Clonidine Premedication in Patients with Sleep Apnea?

### To the Editor:

The recent work on clonidine in sleep apnea by Pawlik et al. (1) is compromised by methodological concerns. Specifically, it is not surprising to find a reduced opioid demand (2), as well as lower mean arterial blood pressure (MAP) and less hypertonic episodes in patients

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